MECHANISMS INVOLVED IN VIP REGULATION OF EMBRYONIC GROWTH.

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VIP regulates embryonic growth during the early postimplantation period, embryonic days (E) 9-11 in the mouse. VIP treatment dramatically stimulates growth which is reflected in a shortening of the cell cycle.

Our current investigations have revealed that VIP treatment of E9 mouse embryos for 2 hours, results in a 2-fold increase in cyclin A and a 1.7-fold increase in cyclin B relative to total RNA. This increase in the expression of cell cycle regulators is consistent with a shortening of the cell cycle.

VIP stimulation resulted in a coordinated growth of both embryo brain and body, even though VIP receptors are restricted to the CNS at this time. This suggests an indirect action of VIP, which is known to stimulate the release of several factors including the novel growth factor, activity dependent neurotrophic factor (ADNF). We now report that treatment of E9 embryos with an antibody to ADNF prevented VIP-induced growth. In addition, we have shown that picomolar concentrations of ADNF stimulated growth of the E9 mouse embryo and that an antibody to ADNF inhibited growth. Treatment of pregnant mice with ADNF antibody induced growth retardation only when treatment occurred during, but not before or after, days 8, 9 or 10 of gestation.

The results of these studies suggest that 1) VIP-stimulated growth occurs through increases in regulators of the cell cycle; 2) ADNF is produced in the embryo or embryonic membranes; 3) ADNF regulates growth during a very limited period of postimplantation; and 4) VIP regulation of embryonic growth is mediated, at least in part, through ADNF.